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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/722,096	11/22/2000	Ernest G. Hope	12531-002001	4236

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EXAMINER	
YAEN, CHRISTOPHER H	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/722,096	HOPE, ERNEST G.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,20-22,24,25,34-58,60,61 and 64-100* is/are pending in the application.

4a) Of the above claim(s) *1,6,20-22,24,25,68-70 and 72-87* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-61,64-67,71, 74, and 88-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/31/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Hope EG
Priority Date: 24 November 1999

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/2004 and 5/7/2004 has been entered.

2. Claims 2-5, 7-19, 23,26-33,59, 62, and 63 are canceled without prejudice or disclaimer. Claims 1,6,20-22,24-25,34-58, 60-61, and 64-100 are pending, claims 1,6,20-22,24-25,68-70, and 72-87 are withdrawn from further consideration as being drawn to non-elected subject matter.

3. Newly submitted claims 1,6,20-22,24-25,68-70, and 72-87 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: An examination has been performed on a composition comprising a population of cytotoxic lymphocytes that are ex vivo expanded in the absence of tumor or vasculature associated antigen. The newly amended claims are drawn to a population of ex vivo expanded cytotoxic lymphocytes, wherein the scope of the expansion is broadened, to include expansion in the presence of an antigen. Had these

claims been presented earlier, these claims would have been subject to a restriction, as being drawn to a different and distinct invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1,6,20-22,24-25,68-70, and 72-87 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. Claims 60-61,64-67,71, 74, and 88-100 are examined on the merits.

Specification

5. The disclosure is objected to because of the following informalities: it is noted that the specification recites a sequence on page 32, line 17 which is not in compliance with the sequence rules set forth under 37 CFR 1.821 - 1.825. Since the sequence is not specifically required or claimed in the instant invention, applicant is required to make correction to comply with the rules set forth in 37 CFR 1.821-1.825 in response to this office action.

Claim Objections

6. Claims 93, and 95-100 are objected to because of the following informalities:

a. Claim 93 is drawn to a claim that is non-elected invention (i.e. claim 1)

b. Claims 95-100 recite method which are dependent of claim 94 which is drawn to a composition.

Appropriate correction is required.

Claim Rejections Maintained - 35 USC § 102

7. The rejection of claims 60-61 and now claims 64-67, 74, 88, and 93-100 under 35 USC 102(b) as being anticipated by Lu *et al* is maintained for the reasons of record. In the response filed 3/8/2004 applicant argues that the means of generating the CIK cells are different in that the time course for the addition of the cytokines and antibodies were different, and further argues that the system used to grow the CIK cells is different from that of the instantly claimed invention. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. The invention is drawn to the product *per se*, and the method of producing the CIK cells involves the addition of the same or similar components. Applicant states that the instant composition does not require the addition of rIL-1α, however, the claims do not specifically preclude the addition of such cytokine in making the composition. Furthermore, because the Office does not have the facilities to determine the difference between the cells of Lu *et al* and those instantly claimed, they are presumed to be the same cells. Furthermore, Applicant has not provided evidence that the product is structurally different from that already taught in the prior art. Moreover, applicant has not set forth any evidence that the "timing" of the cytokine and antibody incubations necessarily generate a different product from that already taught by Lu *et al.* Furthermore, because the cells taught by Lu *et al* appears to be the same as those instantly claimed (i.e. the cells are both CIK cells), the means by which the product is achieved is not deemed a patentable distinction and as such is not patentable *Ex parte Gray 10 USPQ2d 1922 (Bd. Pat App & Inter.* 1989).

Applicant further argues that the examiner over-generalized the function of the CIK cells taught by Lu *et al* in stating that the said cells were able to generate an anti-tumor response, rather the Lu *et al* cells are only capable of eliciting an anti-lymphoma response and has not provided any evidence of being able to treat other cancer cell type or for selective destruction of tumor vascular cells. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. Because the invention is drawn to a product *per se*, the functional limitations applied to the cells taught in the instant invention would be an inherent property and as such would also be a function associated with the cells taught by Lu *et al*. The instant specification has not provided any structurally distinguishing characteristics such that one of skill in the art could differentiate the cells taught by Lu *et al* from the one instantly claimed. While the features of a product can be recited by either structure or function, claims to a product must be distinguished form the prior art by structure rather than by function. *In re Shreiber 128 F.3d 1473, 1447-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997).*

In the response filed 5/7/2004 applicant argues that Lu *et al* fails to teach a subpopulation that expresses one or more members of a cell surface receptor family that binds to HSP47. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. As stated above, the cell population of the instant cannot be distinguished over the cell population taught in the prior art because the process of making the composition of CIK cells of the prior art appears to be identical to that of the instant invention (i.e. the addition of IFN gamma,

anti-CD3 antibody, and IL-2). Moreover, the specification has not specifically defined a structural difference between the CIK cells of Lu *et al* and the cell population claimed in the instant invention such that one of ordinary skill in the art would readily find apparent. The finding of latent/inherent properties within a product is not deemed sufficient to overcome the findings of the prior art. One of ordinary skill in the art would conclude that the cell population taught by Lu *et al* would also have receptors for HSP47 because the process of forming the two cell populations are similar. Therefore, in the absence of factual evidence to the contrary, of which the applicant has not clearly set forth, the composition of cells taught in the instant specification are the same as those taught by Lu *et al*.

With regard to newly rejected claims 64-67, 74, 88, and 93-100, Lu *et al* teaches a population of cytotoxic lymphocytes that are expanded in the absence of an antigen. Because the product taught by Lu *et al* appears to be the same, the functional limitations set forth in claims 65-67,88 are considered inherent properties that are present in a cell that has been prepared in the same manner as that instantly claimed. Lu *et al* also disclosed the administration of an anti-CD3 antibody and IL-2 (see page 1688). Furthermore, because the invention is drawn to a product per se, the method of preparing the population of cells does not breadth any patentable weight into the claims as set forth in claims 96-100. Also, because the Office does not have the facilities to determine if the method of preparing the cells taught by Lu *et al* produces a patentable distinct cell type, in the absence of evidence to the contrary, the cells are the same.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 88-92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth an antibody as an agent, and is therefore not commensurate in scope to the broad class of agents claimed.

The claims recite "an agent" as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature of this "agent". Beyond the mere recitation of an agent, the specification has not taught the identify or the structure of this agent, and therefore one of skill in the art would not be able to determine whether the applicant was in full possession of the invention at the time of the invention was made. The specification has only taught that an "agent" is an antibody and has not taught any other structures or compounds that would fall within the scope of the term. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus

may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice a representative number of species to be entitled to the genus of "agents". Neither has Applicant provided a sufficient written description of any other structure, other than antibodies, that may be correlated with the function of binding to the surface of the cells or acting as a scaffold. An "agent" encompasses *any* molecule with an unlimited number of possible functions. Thus the genus of compounds encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the

subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Claim Rejections - 35 USC § 102

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 60,61,64-67, 74, 88,and 93-100 are rejected under 35 U.S.C. 102(b) as being anticipated by Alvernas JC *et al* (Blood, 1996 November; Vol. 88(10 Supplemental): abstract # 2882). Alvernas *et al* teach a composition comprising ex vivo expanded cells termed CIK cells of which are made by a process of sequential stimulation of mononuclear cells with IFN gamma, anti-CD3 antibody, and IL-2, wherein the CIK cells are selective for endothelial cells, and express CD3 and CD56. Because the specification of the instant invention states that any hematopoietic cell source can be used (see page 9) and that the cells are generated by stimulation with IFN gamma, anti-CD3 antibody, and IL-2, the cells taught by Alvernas *et al* appear to be the same as those claimed by the applicants of the instant invention. Other limitations encompassed by the claims of the instant invention such as selective killing of tumor-associated endothelial cells; cells and subpopulations of cells that do not cause vascular leak syndrome; cells and subpopulations of cells that do not express T cell receptor are considered inherent properties associated with the cells which are made by a specific process. Therefore these functional limitations are also anticipated by Alvernas *et al.* The invention is also claimed as a product by process, such as in claims 94-100,

however, since the product claimed is similar to that already taught by Alvernas *et al* and because the methods of making do not impart any special characteristics in terms of structure to the cellular composition, these limitations do not breadth any patentable weight into the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 60,61,64-67, 71, 74,88,and 93-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alvernas *et al* in view of Bear HD (J Surg Res. 1987 Apr;42(4):369-76.)

a. The teaching of Alvernas *et al* are set forth above as they apply to claims 60,61,64-67, 74, 88,and 93-100.

b. Alvernas *et al* however does not specifically teach the fusion of CIK cells with another cell type.

c. Bear HD teaches the fusion of T-cells with thymoma to generate a hybrid cell.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fuse the ex vivo expanded cytotoxic lymphocyte cell with a thymoma. One of skill in the art would have found motivation in

doing so because Bear HD taught that the fused cells were able to suppress the generation of CTL in an antigen specific manner, while Alvernas *et al* taught that the cytotoxic lymphcytes (herein CIK) were effective in targeting endothelial cells. Thus, one of skill would have found a reasonable expectation in making cells that are antigen specific and specifically targets endothelial cells as claimed because both reference taught successful and effective immune mediation with the different cell types and further suggest that the cells would provide for antigen specific suppression via the hybrid cell

Conclusion

18. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
May 20, 2004

GARY NICKOL
PRIMARY EXAMINER